Viral Infections in Short-Term Injection Drug Users: The Prevalence of the Hepatitis C, Hepatitis B, Human Immunodeficiency, and Human T-Lymphotropic Viruses

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ABSTRACT

Objectives. The purpose of this study was to estimate the prevalence and correlates of four blood-borne viral infections among illicit drug injectors with up to 6 years of injecting experience.

Methods. We analyzed data from 716 volunteers recruited in 1988 and 1989. Test results for hepatitis C virus (HCV), hepatitis B virus (HBV), human immunodeficiency virus, type 1 (HIV), and human T-lymphotropic virus types I and II (HTLV) were examined across six sequential cohorts defined by duration of drug injection.

Results. Overall, seroprevalence of HCV, HBV, HIV, and HTLV was 76.9%, 65.7%, 20.5% and 1.8%, respectively, and 64.7%, 49.8%, 13.9%, and 0.5%, respectively, among those who had injected for 1 year or less. Among the newest initiates, HCV and HBV were associated with injecting variables, and HIV was associated with sexual variables.

Conclusions. The high rates of HCV, HBV, and HIV infections among short-term injectors emphasizes the need to target both parenteral and sexual risk reduction interventions early. Renewed efforts at primary prevention of substance abuse are indicated. (*Am J Public Health.* 1996;86:655–661)

Introduction

Injection drug users are at high risk for infection with several blood-borne pathogens, including hepatitis C virus (HCV),[1] hepatitis B virus (HBV),[2] human immunodeficiency virus, type 1 (HIV),[3] and human T-lymphotropic virus types I and II (HTLV).[4] Transmission is primarily parenteral through the sharing of contaminated injection equipment.[5–8]

An important variable to consider when differentiating risk for these infections within this population is the duration of injection drug use. Cross-sectional surveys tend to show that the prevalence of infection increases with longer duration of injection drug use,[9–11] which likely reflects an effect of cumulative exposure. However, incidence data also show that, for a given calendar time, more recent initiates into injection drug use have higher rates of new infection compared with more experienced drug users.[12–14] This increased risk among newer injectors emphasizes the importance of targeting preventive interventions early for them to be most effective; however, it is not yet clear how early it is necessary to intervene.

To date, studies of viral infections among injection drug users typically grouped data into broad categories. Duration of injecting has been defined as longer or shorter than 5 years[5,9] and as longer or shorter than 2 years.[12] To better understand periods of increased risks for these different viral infections, further refinements in the duration of injecting are needed.

Between February 1988 and March 1989, we recruited 2921 injection drug users into a longitudinal study of HIV infection (the AIDS Link to the Intravenous Experience [ALIVE] Study), of whom 716 reported initiation into injection drug use within the 6 years before enrollment. We conducted a cross-sectional analysis using baseline data stratified into six sequential cohorts defined by duration of injection drug use. These represent mutually exclusive groups. For each cohort, we tested sera for antibodies to HCV, HBV, HIV, and HTLV. The purpose of this study was to evaluate the seroprevalence rates by duration of injecting to identify time periods associated with significant increases in infection rates and to evaluate the effect of important risk correlates reflecting drug use and sexual practices. Assuming that the risk of infection was low before initiation of injection drug use, particularly for HCV,[15] we intended to identify defined time periods after initiation when seroprevalence increased significantly, thereby providing a "window period" during which infection prevention programs could be focused. Pinpointing periods of increased risk provides information for clinicians and public health practitioners so that they can further focus the timing for such interventions.

Methods

The objectives, rationale, and methods of obtaining data on this study population have been described in detail

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elsewhere.[16] In brief, the ALIVE Study, a natural history study of HIV infection among injection drug users, began in February 1988. Volunteers were recruited through word-of-mouth from a variety of community agencies including drug abuse treatment centers, city health department sexually transmitted disease clinics, local emergency rooms, HIV–AIDS clinics, state parole and probation offices, and community AIDS education programs such as the Street Outreach AIDS Prevention Unit of the Health Education Resource Organization. The project staff also distributed brochures describing the study at selected public housing units and other locations alleged to be frequented by injection drug users. Ultimately, over 80% of the participants were recruited through word-of-mouth from friends and contacts. To be eligible for enrollment into the study, volunteers had to be 18 years of age or older, had to have a history of injecting illicit drugs at any time since 1977, and had to be AIDS-free at baseline.

Data Collection

Eligible and consenting participants underwent confidential, face-to-face interviews at 6-month intervals with a trained interviewer. All data for this analysis came from the baseline interview. The baseline interview elicited data on demographics, medical history, injection drug use, and sexual behaviors. To minimize the possibility that information on risk reduction would alter self-reports about risk activities, HIV prevention counseling was administered after the interview but before participants left the clinic. Participants were modestly reimbursed for their time and scheduled to return for HIV test results. The study procedures were approved by the Institutional Review Board of the Johns Hopkins School of Hygiene and Public Health.

Laboratory Analysis

All laboratory testing was performed on sera collected at the baseline visit. Sera from all 716 participants were tested for HBV, HIV, and HTLV; however, due to high costs and relative newness of the assay, HCV testing was performed on only 312 of these participants. In addition to a group of HIV-positive participants that were randomly selected for another study of liver disease, only persons who were still alive and participating in the study in 1991 had HCV testing done on their baseline sera.

For a preliminary study, approximately 20% of the serum samples were tested for antibody to HCV (anti-HCV) with a commercially available first-generation enzyme-linked immunosorbant assay (ELISA) (Ortho Diagnostics, Raritan, NJ) according to the manufacturer's specifications. Specimens that were repeatedly reactive by ELISA and that had optical densities less than four times the cutoff were confirmed by a first-generation recombinant immunoblot assay HCV Test System (Chiron Corporation, Emeryville, Calif, and Ortho Diagnostics). The remaining sera were tested with a second-generation Ortho HCV ELISA. Because in the preliminary testing over 95% of the repeatedly reactive specimens were also positive by the recombinant immunoblot assay, specimens repeatedly reactive by the second-generation ELISA (which has at least equal specificity) were considered positive without additional testing.

Baseline serum specimens were tested for HBV surface antigen (HBsAg) and antibody (anti-HBs) and antibody to HBV core antigen (anti-HBc) by ELISA (AUSZYME, AUSAB, and CORZYME, respectively; Abbott Laboratories, North Chicago, Ill). For the purpose of this analysis, participants were considered HBV positive when they had a confirmed test for any of these markers. A more detailed analysis of HBV markers for this population has been described elsewhere.[2]

Serum specimens were assayed for antibody to HIV with ELISA (Genetic Systems, Seattle, Wash) and Western blot (Biotech–DuPont, Rockville, Md). All repeatedly reactive specimens with ELISA were assayed by Western blot; a positive Western blot was defined as a band at either a *gag* (p56, p24, or p17) or *pol* (p66, p31, or p51) gene product and a band at an *env* (gp41, gp120 or gp160) gene product. No equivocal tests were obtained with these criteria.

Serum specimens were screened for antibody to HTLV by ELISA (HTLV-1 rgp21e, Cambridge Bioscience, Worchester, Mass). Repeatedly reactive specimens were confirmed by immunoblot that incorporated rgp21e (Cambridge Biotech, Rockville, Md). The minimum criterion for seropositivity was the presence of antibodies to rgp21e and p24 proteins.

Sera from all subjects were tested for HIV immediately after the baseline interview. Tests for HCV, HBV, and HTLV infections were performed in batch at later dates as funding became available with sera that had been stored at −70°C and thawed just before testing.

Data Analysis

This cross-sectional analysis was restricted to 716 participants who reported the year of first injection as 1983 through 1988 (the year the baseline interview was conducted) to focus on recently initiated (i.e., within the preceding 6 years) injection drug users. Duration of injecting was calculated as the period of time from a participant's reported first injection to his or her last injection. Although in most cases the years of duration corresponded with the calendar year of initiation, the computed duration was considered more accurate, because 13.8% of participants were not currently injecting (i.e., had not injected within the 6 months before the baseline interview). The distribution of demographic characteristics among former and current users was not statistically different; therefore, subsequent analyses combined former and current users.

For the first part of this analysis, data were divided into six mutually exclusive cohorts defined by duration of injecting, such that the first cohort included those who injected for 0 to 12 months, the second cohort included those who injected for 13 to 24 months, and so on up to a sixth cohort with an injection duration of 61 to 72 months. Seroprevalence of antibodies to HCV, HBV, HIV, and HTLV was measured for each sequential cohort. To measure trends and maintain uniform sample sizes in each group, the first year was further divided into 4-month intervals.

In the second part of this analysis, we were interested in identifying correlates of infection among those who had injected for 1 year or less. The rationale for conducting detailed analyses on the subgroup with less than 1 year of injection includes finding that the largest increase in HCV and HBV infection was during this period, the sample size was sufficient for meaningful analysis, and the baseline questionnaire probed into recent (i.e., 6 months before last injection) behaviors, which were more relevant to consider within a restricted time frame. Demographic, drug use, and sexual behavior data were available for analysis. Demographic variables included age (18–25 years old vs >25 years old), education (<12 years vs ≥ 12 years), annual legal income ($<$ US \$5000 vs $\geq$ US \$5000), sex, and race. Although participants were not selected on the basis of race, 88% were

Black and nearly all of the remaining participants were White; therefore, race was grouped into Black and non-Black.

Visible injecting scars (stigmata) observed at the time of the baseline blood sample were recorded as a marker of and validation for self-reported injection drug use. The proportion of participants with a history of treatment for drug abuse (yes vs no) was compared across cohorts as a measure of construct validity for self-reported duration of injecting because we expected that the proportion reporting a history of treatment would increase with increasing duration. For the 6 months before last injection, we assessed the frequency of injecting (once or more daily vs less than daily, used previously to define addiction[17]), the injection of any cocaine (yes vs no), and use of needles that came from sealed sterile wrappers just before injecting (always vs less often than always). Frequency of using new needles from a sealed sterile wrapper was chosen to measure needle sharing to circumvent difficulties in the measurement of needle sharing with or without bleach disinfection.[18]

Marital status (ever vs never married) was included as a surrogate marker for economic, social, and sexual stability. Male participants who reported sex with at least one male during the 10 years before baseline, regardless of also reporting sex with females, were listed as homosexual or bisexual. The one female participant who reported having sex exclusively with females was excluded from the analysis. Having sex with an injection drug user during the 10 years before the interview was dichotomized. The distribution of reported number of sex partners during the past 10 years (range, 1–512) had no natural breaks, so the median was chosen to dichotomize this variable for analysis (≤ 5 partners vs > 5 partners).

Statistical Analysis

Frequency distributions of demographic variables were stratified by antibody status and duration of injection drug use at baseline. Chi-square and Fisher's Exact statistics were used to guide interpretations.[19] Trends in the seroprevalence by duration of injection drug use were analyzed by using the Mantel–Haenszel test for trends. Trends of infection by duration of injecting were then stratified by age (18–25 years old vs > 25 years old), and logistic regression with an interaction term for age and duration was used to formally test differences between injectors above and below 25 years old. To evaluate the univariate associations between demographic and behavioral information with antibody status for persons who had injected for 1 year or less, we calculated chi-square statistics using a P value of .05 and odds ratios with 95% confidence intervals to guide interpretations. We made simultaneous comparisons of risk factors for seropositivity using multiple logistic regression.[20]

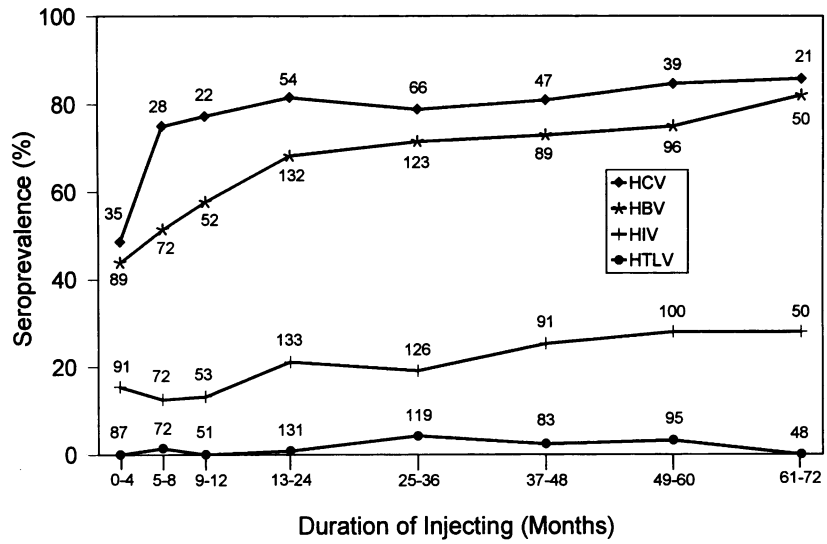
TABLE 1—Baseline Characteristics of Injection Drug Users Who First Injected between 1983 and 1988, by Duration of Injecting: ALIVE Study, Baltimore, Md

	Months of Injection Drug Use					
	0–12 (n = 216)	13–24 (n = 133)	25–36 (n = 126)	37–48 (n = 91)	49–60 (n = 100)	61–72 (n = 50)
Median age, y (range)	28.5 (18–57)	28.7 (18–55)	28.4 (19–51)	29.2 (19–60)	28.8 (19–50)	28.1 (22–41)
Sex, %						
Male	74.5	73.7	72.2	76.9	67.0	64.0
Female	25.5	26.3	27.8	23.1	33.0	36.0
Race, %						
Black	89.8	85.0	88.9	86.8	87.0	90.0
Other	10.2	15.0	11.1	13.2	13.0	10.0
Education, %						
<12 y	58.8	59.4	63.5	57.1	62.0	56.0
≥ 12 y	41.2	40.6	36.5	42.9	38.0	44.0
Annual income, %						
$<\$5000$	74.5	76.5	76.0	75.6	72.7	81.6
$\geq \$5000$	25.5	23.5	24.0	24.4	27.3	18.4
Ever married, %						
Yes	26.9	16.5	24.6	26.4	23.0	20.0
No	73.2	83.5	75.4	73.6	77.0	80.0
Sexual orientation, %						
Male heterosexual	69.0	66.2	65.1	69.2	57.0	56.0
Male bisexual or homosexual	5.6	7.5	7.1	7.7	10.0	8.0
Female (combined)	25.5	26.3	27.8	23.1	33.0	36.0

Results

Of the 2921 intravenous drug users enrolled into the ALIVE Study, 716 reported injecting drugs for 72 months or less before the interview. Table 1 shows the distributions for selected baseline characteristics of these 716 participants stratified by duration of injecting in years. Ten percent of the males had sex at least once with another male; however, fewer than 1% reported having sex exclusively with males. The distributions of age, sex, race, education, income, marital status, and sexual orientation did not differ significantly across the six sequential cohorts defined by injecting duration. A statistically significant chi-square test for linear trend was observed for an increasing proportion of participants who had a history of treatment for drug abuse with increasing duration of drug use ($P = .001$). Injecting stigmata were observed in 82% of the participants; therefore, we were reasonably confident of the overall validity of self-reported injection drug use.

Serologic testing was performed on 312, 703, 716, and 686 participants for HCV, HBV, HIV, and HTLV, respectively. Thirteen and 30 participants were not tested for HBV and HTLV, respectively, due to unavailability of sera. No important differences were observed between those who were not tested and those who were tested, but for HCV we noted the following. Out of 716 participants, the 312 with HCV testing were more likely to be Black, to be currently injecting, to possess visible stigmata, and to test positive for HIV ($P < .05$ for each by the two-tailed chi-square test). Out of 216 participants who had injected for 1 year or less, the 85 with HCV testing were more likely to be Black ($P = .002$) and currently injecting ($P = .006$), whereas being heterosexual ($P = .053$), injecting daily ($P = .063$), and possessing stigmata ($P = .052$) were only marginally significant.



Note. The sample sizes used to calculate seroprevalence rates are adjacent to the data points.

FIGURE 1—The prevalence of hepatitis C virus (HCV), hepatitis B virus (HBV), human immunodeficiency virus (HIV), and human T-lymphotropic virus (HTLV) infection in serial cohorts with increasing duration of injection drug use: the ALIVE Study, Baltimore, Md, 1983 through 1988.

Overall, the crude seroprevalence of HCV, HBV, HIV, and HTLV was 76.9%, 65.7%, 20.5%, and 1.8%, respectively, for the 716 participants with up to 6 years of injection drug use. Of the 216 participants with 1 year or less of injection drug use, 64.7%, 49.8%, 13.9%, and 0.5% were seropositive for HCV, HBV, HIV, and HTLV, respectively. Across the six sequential cohorts, there was a dramatic increase in the prevalence of HCV and HBV infections within the first 2 years, but a more modest increase in the rate of HIV infection (Figure 1). Independent chi-square tests for linear trend by duration of injecting were highly significant for HCV, HBV, and HIV ($P < .002$); however, HTLV infection appeared essentially unchanged ($P = .533$). Although seroprevalence was high for both HCV and HBV, for those who had injected for 0 to 4 months compared with those who had injected for 9 to 12 months, there was a more dramatic increase in the seroprevalence for HCV than for HBV.

Stratified analysis of participants 18 to 25 years old and more than 25 years old showed some variability in the seroprevalence of all four viruses for each level of duration. However, using logistic regression we found that the differences between the two age groups were not statistically significant for any of the four infections. Also, the association between infection and duration of injecting was not modified by age.

We examined possible correlates for these infections. Limiting the analysis to participants who had injected drugs for 1 year or less and had complete data for all variables of interest left 78, 200, and 203 participants for HCV, HBV, and HIV, respectively. Only one participant who had injected for 1 year or less was found to be positive for HTLV, thereby precluding a meaningful analysis of correlates for HTLV infection. Tables 2 and 3 show univariate associations between risk characteristics and a positive test for HCV, HBV, or HIV in participants who injected for 1 year or less.

Infection with HCV and HBV among those with up to 1 year of injection drug use were associated with higher-risk injection variables (Table 2), but not with sexual variables (Table 3). HCV and HBV were each associated with injecting daily during the past 6 months, injecting cocaine during the past 6 months, and injecting for 7 to 12 months vs 6 months or less. Use of needles that came from a sealed sterile wrapper less often than always during the past 6 months had a significant association with seropositivity for HCV but not for HBV. There were no statistically significant associations between HCV or HBV and sex, marital status, total number of sex partners in the past 10 years, having sex partners in the past 10 years who were known to be injection drug users, or sexual orientation. Age was marginally significant for HBV but not for HCV. A greater proportion of Black participants than non-Black participants were seropositive for HCV and HBV, though these differences were not statistically significant. Total number of sex partners was stratified with the median, tertiles, quartiles, and more than 10 partners as cut points, yet this variable remained nonsignificant for HCV and HBV seroprevalence.

Infection with HIV among those with up to 1 year of injecting was associated with sexual variables (Table 3), but not with higher-risk injection variables (Table 2). Having never been married and being a male who had sexual intercourse with males were both significantly associated with HIV infection. Age, sex, race, total number of sexual partners during the past 10 years, and number of sex partners during the past 10 years who were known to have injected drugs were not associated with HIV seropositivity. HIV seropositivity was not associated with any of the high-risk drug use variables we evaluated (Table 2), although injecting cocaine during the past 6 months was suggestive.

To simultaneously adjust for factors found to be associated with HCV, HBV, or HIV on univariate analyses, we evaluated several logistic regression models using HCV, HBV, and HIV as dependent variables. In the final models (Table 4), daily injection, injection of cocaine during the past 6 months, and injecting for more than 6 months all were associated with an increase in the relative odds of seroprevalence for HCV and HBV. Using needles that came from a sealed sterile wrapper less often than always was no longer statistically significant for HCV after adjustment for the other three variables in the multivariate model and was excluded from the final model. Controlling for high-risk drug use activities did not significantly alter the strength of association between sexual activity and HCV or HBV.

The final model for HIV infection included only marital status and sexual orientation. Never having been married and being a homosexual or bisexual male contributed independently to an increase in the relative odds of HIV seropositivity. Adjusting for age, sex, race, and drug use variables did not significantly alter the strength of these associations, nor did

TABLE 2—Univariate Analysis of Drug Use Variables for Infection with HCV, HBV, and HIV among Participants with 12 or Fewer Months of Injection Drug Use: ALIVE Study, Baltimore, Md, 1983 through 1988

	HCV			HBV			HIV		
	No.	%	OR (95% CI)	No.	%	OR (95% CI)	No.	%	OR (95% CI)
Injection frequency in last 6 mo									
Less than daily	58	56.9	1.00	165	46.1	1.00	167	14.4	1.00
Once or more daily	20	85.0	4.29 (1.2, 15.3)	35	68.6	2.56 (1.2, 5.5)	36	13.9	0.96 (0.3, 2.7)
Injected any cocaine in last 6 mo									
No	13	30.8	1.00	42	33.3	1.00	42	7.1	1.00
Yes	65	70.8	5.45 (1.6, 18.4)	158	54.4	2.39 (1.2, 4.8)	161	16.2	2.50 (0.7, 8.4)
Duration of IDU, mo									
0–6	50	54.0	1.00	125	42.4	1.00	127	14.2	1.00
7–12	28	82.1	3.92 (1.3, 11.6)	75	62.7	2.28 (1.3, 4.1)	76	14.5	1.03 (0.5, 2.3)
Needle from sterile wrapper in last 6 mo									
Always	20	45.0	1.00	54	42.6	1.00	54	13.0	1.00
<always	58	70.7	2.95 (1.1, 8.3)	146	52.7	1.50 (0.8, 2.8)	149	14.8	1.16 (0.5, 2.9)

Note. OR = odds ratio; CI = confidence interval; HCV = hepatitis C virus; HBV = hepatitis B virus; HIV = human immunodeficiency virus; IDU = injection drug use.

TABLE 3—Univariate Analysis of Demographic and Sexual Variables for Infection with HCV, HBV, and HIV among Participants with 12 or Fewer Months of Injection Drug Use: ALIVE Study, Baltimore, Md, 1983 through 1988

	HCV			HBV			HIV		
	No.	%	OR (95% CI)	No.	%	OR (95% CI)	No.	%	OR (95% CI)
Race									
Non-Black	2	0.0	1.00	21	38.1	1.00	22	4.6	1.00
Black	76	65.8	9.53 (0.4, 205.8)	179	51.4	1.72 (0.7, 4.3)	181	15.5	3.84 (0.6, 26.01)
Age, y									
18–25	20	80.0	1.00	60	40.0	1.00	62	9.7	1.00
>25	58	58.6	0.35 (0.1, 1.2)	140	54.3	1.78 (1.0, 3.3)	141	16.3	1.82 (0.7, 4.7)
Sex									
Female	24	58.3	1.00	51	49.0	1.00	51	11.8	1.00
Male	54	66.7	1.43 (0.5, 3.9)	149	50.3	1.05 (0.6, 2.0)	152	15.1	1.34 (0.5, 3.5)
Ever married									
Yes	18	50.0	1.00	55	60.0	1.00	56	5.4	1.00
No	60	68.3	2.16 (0.7, 6.3)	145	46.2	0.57 (0.3, 1.1)	147	17.7	3.80 (1.2, 12.2)
No. sex partners in last 10 years									
1–5	30	60.0	1.00	85	56.5	1.00	85	12.9	1.00
>5	48	66.7	1.33 (0.5, 3.5)	115	45.2	0.64 (0.4, 1.1)	118	15.3	1.21 (0.5, 2.7)
Sex with injection drug user in last 10 years									
No	25	72.0	1.00	66	57.6	1.00	67	11.9	1.00
Yes	53	60.4	0.59 (0.2, 1.7)	134	46.3	0.64 (0.4, 1.2)	136	15.4	1.35 (0.6, 3.2)
Sexual orientation									
Heterosexual	77	64.9	1.00	189	49.2	1.00	192	12.5	1.00
Homosexual and bisexual	1	0.0	0.18 (0.0, 4.6)[a]	11	63.6	1.81 (0.5, 6.3)	11	45.5	5.83 (1.9, 18.3)

Note. OR = odds ratio; CI = confidence interval; HCV = hepatitis C virus; HBV = hepatitis B virus; HIV = human immunodeficiency virus.
[a]Mantel–Haenszel logit estimators use a correction of 0.5 for cells that contain zero.

controlling for marital status and/or sexual orientation increase the association of any drug use variables with HIV infection.

Given the high rate of HCV infection in the 0- to 4-month group, we attempted to look for other factors that could suggest infection before initiation (such as history of blood transfusion since 1977); for the 10 years before baseline, we looked at history of sex with an injection drug user, sex for money or drugs, sex with anonymous partners (asked of males only), homosexual or bisexual activity, sexually transmitted diseases, number of sexual partners, and arrest or incarceration. However, none of these factors were found to be associated with HCV infection among the very short duration injection drug users.

TABLE 4—Multiple Logistic Regression Analysis of Factors Associated with Prevalent HCV, HBV, or HIV Infection among Injection Drug Users Who Had Injected for 12 or Fewer Months: ALIVE Study, Baltimore, Md, 1983 through 1988

Independent Variables	Unadjusted OR	Adjusted OR	Adjusted 95% CI
HCV (n = 78)[a]			
Injected daily vs less than daily	4.29	4.40	1.01, 19.10
Injected any cocaine in last 6 mo vs no cocaine injected	5.45	5.25	1.24, 22.22
Duration of injection drug use 7–12 mo vs 0–6 mo	3.92	5.30	1.46, 19.20
HBV (n = 200)[b]			
Injected daily vs less than daily	2.56	2.37	1.05, 5.33
Injected any cocaine in last 6 mo vs no cocaine injected	2.39	2.18	1.03, 4.59
Duration of injection drug use 7–12 mo vs 0–6 mo	2.28	2.14	1.17, 3.94
HIV (n = 203)[c]			
Never married vs ever married	3.80	4.00	1.12, 14.29
Homosexual or bisexual male vs heterosexual	5.83	5.52	1.38, 22.17

Note. OR = odds ratio; CI = confidence interval; HCV = hepatitis C virus; HBV = hepatitis B virus; HIV = human immunodeficiency virus.
[a]HCV model included age (OR = 0.35; CI = 0.09, 1.35) and sex (OR = 1.07; CI = 0.33, 3.43). Race was not included as 97.4% were Black.
[b]HBV model included age (OR = 1.75; CI = 0.91, 3.33), sex (OR = 0.93; CI = 0.55, 1.82), and race (OR = 1.43; CI = 0.53, 3.86).
[c]HIV model included age (OR = 2.43; CI = 0.89, 6.61), sex (OR = 0.94; CI = 0.34, 2.59), and race (OR = 2.93; CI = 0.36, 23.72).

Discussion

A major finding of this study was high rates of blood-borne viral infections observed within the first 6 years after initiating injection drug use. Among the cohort with 49 to 72 months of injecting history, we found that the seroprevalence rates for HCV, HBV, HIV, and HTLV (85.0%, 77.4%, 28.0% and 2.1%, respectively) were similar to rates for the overall ALIVE Study cohort (85.3%,[15] 84.0%,[6] 24.1%,[16] and 7%,[21] respectively), in whom the median duration of injecting at baseline was 12 years.[16] With the exception of HTLV, these findings suggest that most of the transmission occurred within the first 6 years of injection drug use.

Second, within the first 6 years we found that seroprevalence rates for HCV, HBV, and HIV increased with increasing duration of injecting, which could not be explained by the distributions of age, sex, race, education, income, marital status, or sexual orientation across cohorts defined by duration of injecting. Thus, although the data represent six sequential, mutually exclusive cohorts, the observed trends could not be immediately dismissed as being due to differing demographic or behavioral distributions.

The steep trajectory in seroprevalence of HCV and HBV within the first year suggests that most new infections occurred very soon after initiation of injection drug use. This inference is supported further with separate logistic regression analyses of HCV and HBV that were limited to participants with injection durations less than or equal to 1 year; both analyses showed that seropositivity was associated with higher-risk injecting practices but not with sexual activity. The rate of increase and overall seroprevalence for HCV were greater than those for HBV, even though the reported transmissibility of HCV from studies of exposed health care workers appears to be substantially lower than that for HBV.[7] Higher levels of chronic carriage among HCV cases (50%–90%) compared with HBV cases (5%–10%) may have contributed to these findings. For HCV, the initially high and dramatically increasing seroprevalence within the first year, combined with being associated with injection frequency, is consistent with previous literature suggesting that HCV is readily transmitted parenterally,[15] whereas nonparenteral exposures have been found to be inefficient for transmission.[22] Although HBV is considered to be transmitted efficiently by both sexual and parenteral routes, the observed rapid increase in seroprevalence within the first year of injecting, combined with identification of injection frequency and cocaine injecting as predominant correlates for infection, suggests that rapid parenteral transmission of HBV also occurs soon after initiation.

In contrast, the trajectory for HIV seroprevalence increased gradually over the first 2 years, suggesting that HIV was not spread as efficiently as HCV and HBV. Indeed, marital status and sexual orientation, but not high-risk drug use activities, were significantly associated with HIV seroprevalence among those who had injected drugs for up to 1 year. Seroprevalence of HIV reached a rate similar to that in the overall ALIVE Study cohort by the sixth year. As observed by others,[23] our data suggested that injecting cocaine was associated with HIV infection, but this association was not statistically significant. Although the number of infectious carriers in the drug-using community is different for each infection, our data are consistent with other studies that indicate that transmission of HIV is less efficient than transmission of HCV or HBV among injecting drug users. Considering the comparatively gradual increase in the seroprevalence of HIV in the 6 years after initiation of injection drug use, the already-high seroprevalence in the first 4 months of injecting (combined with an estimated incubation period of 2 months), and the fact that HIV infection was primarily associated with sexual variables among those who injected for 1 year or less, our findings suggest that some infections probably occurred via sexual activity and perhaps before injecting drugs. After the second year of injection drug use, however, the observed increase in HIV seroprevalence was consistent with a predominant contribution from parenteral transmission.

The seroprevalence of HTLV was low across the cohorts, which is consistent with the low rate observed in the total ALIVE Study population. The slow rise in HTLV seroprevalence to only 2.1% by 5 to 6 years of injecting might have resulted from a limited reservoir, inefficient transmission, or other factors such as forming new networks of injecting partners. We found the prevalence of HTLV infection to be 0.5% among those who injected 1 year or less, which was similar to the 0.4% seroprevalence reported among patients at a sexually transmitted disease clinic in Baltimore.[24]

The high seroprevalence of HCV, HBV, and HIV observed shortly after initiating injection drug use is disturbing. We considered the possibility that the high rates observed might have been due

to errors or distortions in recall about duration of injecting, such that some recent initiates might have injected for longer durations than reported. Although earlier studies have noted that year or age of initiation tends to be recalled vividly, we noted that the median age of initiation in our cohort (29 years old) was older than that previously reported (20 years old).[17] This probably reflects the fact that the minimum age criteria for study entry was 18 years old in order to meet restrictions of our Institutional Review Board, leading to exclusion of younger initiates and thereby shifting the median age upward. However, to examine the potential for bias, we repeated analyses stratified by age (18–25 vs >25 years old) and found similar results. This result suggests that problems with self-reporting of age at initiation are unlikely to account for our findings.

Caution must be taken when using seroprevalence rates to determine when persons are at highest risk of infection because the actual date of infection is unknown. In addition, the extent to which these data derived from a volunteer sample are generalizable to injection drug users in Baltimore or elsewhere is unknown. Another limitation is the small number of variables examined. The ALIVE Study was not originally designed to investigate new injectors, and a range of possible variables suggested by others need to be considered in future studies.[17] Finally, the subset tested for anti-HCV differed from those not tested; however, the extent of bias cannot be estimated on the bases of the observed differences.

Although it is difficult to conclusively disentangle the reasons for the high prevalence of HCV, HBV and HIV infection found so early after initiation, these data strongly suggest that the early period of injection drug use is particularly dangerous for infection with blood-borne viruses. Given these findings, intervention efforts should be expanded to target injectors and those at risk of starting to inject. We realize that this is a particularly difficult population to reach for a number of reasons, including a person's hesitance to self-identify as an injector and the fact that many new injectors are young and may not be linked to health care or drug treatment services. One alternative would be to train current users to teach their initiates how to avoid risky behaviors. This practice might be expected to decrease the incidence of HCV and HBV that occurs soon after initiation, and if a norm becomes established, this norm might also prevent some HIV and HTLV transmission from occurring later. Given the high levels of infection within the first year of injecting, these data provide an additional rationale to reemphasize the need for primary substance abuse prevention. Also, using HCV or HBV infection as a surrogate for measuring the effectiveness of intervention programs designed to decrease the risk of HIV infection may be impractical when the majority of injection drug users are seropositive within the first year of injecting. Finally, interventions designed to decrease the incidence of HIV infection need to emphasize reduction of risky sexual behaviors as well as high-risk drug-using practices. □

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